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09/615,437	07/13/2000	Christopher M. Kim	CKIM 3.0-001	3371

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EXAMINER
HUYNH, PHUONG N

ART UNIT	PAPER NUMBER
1644	15

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/615,437	Applicant(s) KIM, CHRISTOPHER M.	
	Examiner " Neon" Phuong Huynh	Art Unit 1644	

-- The MAILING DATE of this communication appears on the cov r sh et with the correspondenc address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *Three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 April 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *31-49* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *31-49* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Claims 31-49 are pending.

2. The following new grounds of objection and rejections are necessitated by the amendment filed 4/11/02.

3. Claims 31-41 are rejected under 35 U.S.C. 112, first paragraph, containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This is a new matter rejection.**

Claims 31-41 as written represent a departure from the specification and the claim as originally filed. The specification and the claims as originally filed do not provide a clear support for "wherein the administration of bee venom and anesthetic reduces visual analog scale of the patient by **at least 57**" recited in claim 31.

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

5. Claims 31-41 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The recitation of "reduces visual analog scale of the patient by at least 57" in claim 31 is ambiguous and indefinite. One of ordinary skill in the art cannot appraise the metes and bounds of the claimed invention.

The recitation of "reduces visual analog scale of the patient by to 28 or less" in claim 41 is ambiguous and indefinite. One of ordinary skill in the art cannot appraise the metes and bounds of the claimed invention.

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office Action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claims 31-37, 39 and 41 are rejected under 35 U.S.C. 102(b) as being anticipated by Steigerwaldt *et al.* (1966, AS on PTO 1449).

Steigerwaldt *et al* teach a method of administering bee venom to a patient suffering from a condition such as Rheumatoid arthritis comprising administering to a patient simultaneously between 0.06 mg and 1.62 mg per injection of bee venom intradermally which is about 0.01 mg and about 1.0 mg per injection and one local anesthetic such as procaine hydrochloride in an amount of 0.2%, (that is 0.2 g/100 ml or 2 mg/ml) multiply by 0.1 cc or 0.1 ml per injection which is equivalent to 0.2 mg per injection which is about 0.3 mg per injection (See page 1047, column 1, Standardized Bee Venom, column 2 second paragraph, in particular). The Bee venom is dissolved or suspended in a liquid carrier such as an isotonic solution (See page 1047, 1047, column 1, Standardized Bee Venom, in particular). The reference solution is sufficient to provide 6 mg/ml (0.06 mg /0.1 ml *10), which is between 0.1 mg and 10.0 mg of bee venom per ml or about 5.0 mg per ml. The reference method of administered bee venom in an amount of 0.06 mg and 0.54 mg which is about 0.05 mg and about 0.5 mg per injection (See page 1047, column 2, dosage schedule, in particular). The reference method teaches injecting bee venom in an amount of 0.18 mg, which is about 0.1 mg per injection (See page 1047, column 2, dosage schedule, in particular). The reference method also teaches administering an anesthetic such as procaine hydrochloride in an amount of 0.2% or 0.2 mg per injection, which is about 0.1 mg to about 0.3 mg per injection (See page 1047, column 1, in particular). Because the reference method uses a composition comprising the bee venom and the local anesthetic in the same range as the claimed composition, the reference composition inherently also reduces irritation, and inflammation of the patient which can be measure or visualize using an analog scale by at least 57 or to 28 or less. Thus, the reference teachings anticipate the claimed invention.

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 103(a) that form the basis for the rejections under this section made in this Office Action:

A person shall be entitled to a patent unless:
(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. Claims 31 and 38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Steigerwaldt *et al* (1966, AS on PTO 1449) in view of Cerrati *et al* (A Therapeutic bee sting? Alternatives Complemetary Therapies page 57-58, Aug 1998; PTO 892).

The teachings of Steigerwaldt *et al* have been discussed supra.

The claimed invention as recited in claim 38 differs from the reference only by the recitation that the patient is suffering from Multiple Sclerosis, and rheumatoid arthritis.

Cerrati *et al* teach the benefit of honeybee venom therapy includes rheumatoid arthritis, and multiple sclerosis. Cerrati et al teach melittin slows down the body's inflammatory response inhibiting the amount of free radicals generated by tissues (See page 57, column 1, in particular). Cerrati *et al* teach the positive effects of bee venom on MS include less fatigue and fewer muscle spasms (See page 57, column 2, in particular).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to include patient suffering from MS as taught by Cerrati *et al* for a method of reducing pain by administering bee venom to a patient in need of such treatment as taught by Steigerwaldt *et al.* From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable of success in producing the claimed invention.

One having ordinary skill in the art at the time the invention was made would have been motivated to do this because Cerrati *et al* teach the positive effects of bee venom on MS includes less fatigue and fewer muscle spasms (See page 57, column 2, in particular) and melittin slows down the body's inflammatory response inhibiting the amount of free radicals generated by tissues (See page 57, column 1, in particular).

10. Claim 40 is rejected under 35 U.S.C. 103(a) as being unpatentable over Steigerwaldt *et al* (1966, AS on PTO 1449) in view of Cerrati *et al* (A Therapeutic bee sting? Alternatives Complemetary Therapies page 57-58, Aug 1998; PTO 892) as applied to claims 31 and 38 mentioned above, and further in view of U.S. Patent 6,029,863 (Of record, Feb 2000, PTO 892) or Pharmaceutical Formulary (March 2000 edition, pages 291-292, PTO 892).

The teachings of Steigerwaldt *et al* and Cerrati *et al* have been discussed supra.

The claimed invention as recited in claim 40 differs from the reference only by the recitation that the local anesthetic is lidocaine.

The '863 patent teaches the use of local anesthetic such as 2 to 4% lidocaine as local anesthetic to reduce the pain and discomfort caused by the bee stings thereby "calming" the victim (See column 2, lines 6-10, column 2, line 55, in particular).

The pharmaceutical formulary teaches injectable local anesthetic such as lidocaine for injection as well as topical application (See page 291-292).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute the procaine hydrochloride as taught by Steigerwaldt *et al* with the lidocaine as a local anesthetic as taught by the '863 patent or the pharmaceutical formulary for a method of reducing pain by administering bee venom to a patient in need of such treatment as taught by Steigerwaldt *et al* and Cerrati *et al.* From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable of success in producing the claimed invention.

One having ordinary skill in the art at the time the invention was made would have been motivated to do this because the '863 patent teaches lidocaine as local anesthetic can reduce the pain and discomfort caused by the bee stings thereby "calming" the victim (See column 2, lines 6-10, column 2, line 55, in particular). The pharmaceutical formulary teaches various forms of local anesthetic such as lidocaine which can be injectable or apply topically (See page 291-292).

Applicants' arguments filed 4/11/02 have been fully considered but are not found persuasive.

Applicants' position is that Steigerwaldt does not discloses each and every element of any of new claims 31-49 and does not disclose the use of anesthetic and bee venom to reduce the visual analog scale of the patient by at least 57.

However, Steigerwaldt et al teach the use of anesthetic and bee venom to reduce pain associated with rheumatoid arthritis as discussed supra and the reference treatment inherently reduces visual analog scale of the patient by at least 57.

11. Claims 42-49 are rejected under 35 U.S.C. 103(a) as being unpatentable over Steigerwaldt *et al* (1966, AS on PTO 1449) in view of Banks *et al* (Chemistry and Pharmcology of Honey-bee venom In: Piek T, ed. Venoms of the Hyemoptera. London: Academic Press; 1986, pages 329-416. PTO 892).

The teachings of Steigerwaldt *et al* have been discussed supra.

The claimed invention as recited in claim 42 differs from the reference only by the recitation that the bee venom comprises about 40%-50% of melittin or about 1.5-2% of hyaluronidase in dry weight or wherein the venom exhibits about 40 to about 100 HHU/ml of Hayalouronidase activity when diluted to 100mcg/ml or is capable of inhibiting gelatin induced aggregation of erythrocytes of about 3-5mm/H.

The claimed invention as recited in claim 43 differs from the reference only by the recitation that the bee venom further comprises about 1.5-2.0% of hyaluronidase in dry weight.

The claimed invention as recited in claim 44 differs from the reference only by the recitation that the bee venom exhibits about 40 to 100HHU/ml of Hyaluronidase when dilute to about 100mcg/ml.

The claimed invention as recited in claim 45 differs from the reference only by the recitation that the bee venom is capable of inhibiting gelatin induced aggregation of erythrocytes of about 3-5mm/H.

The claimed invention as recited in claim 46 differs from the reference only by the recitation that the bee venom includes between about 80 to about 9,5000mcg total protein per ml.

The claimed invention as recited in claim 47 differs from the reference only by the recitation that the bee venom contains between about 0.01 to about 0.10mg of melittin and about 400 to about 4,500 mcg total protein per ml.

The claimed invention as recited in claim 48 differs from the reference only by the recitation that the bee venom contains between about 0.04 to about 0.05mg of melittin and about 800 to about 950mcg total protein per ml.

The claimed invention as recited in claim 49 differs from the reference only by the recitation that the bee venom comprises about 40% - 50% of melittin.

Bank *et al* teach melittin is the major component of bee venom, which accounts for about 40%-50% in dry weight, and hyaluronidase accounts for about 1-2% in dry weight of the whole venom (See page 349, Melittin, page 344, Table II, page 337, in particular). Bank *et al* teach commercially available bee venom is that of the common European honeybee Apis melifera and some 98% of the dry weight of bee venom are known (See page 334, first paragraph, page 335, last paragraph, in particular). Bank et al teaches Melittin has anti-inflammatory mechanism and this may be why therapeutic properties have long been attributed to bee venom, especially in arthritic conditions (Seep age 403, first paragraph, in particular). Bank *et al* teach that starting

with 50 mg, only 1 mg of hyaluronidase could be produced if the purification produced a 100% yield (See page 344, second paragraph, in particular).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute the bee venom as taught by Steigerwaldt *et al* for the venom comprises about 40%-50% of melittin or about 1.5-2% of hyaluronidase in dry weight as taught by Bank *et al* for a method of administering bee venom to a patient simultaneously between 0.06 mg and 1.62 mg per injection of bee venom intradermally, which is about 0.01 mg and about 1.0 mg per injection and one local anesthetic wherein the bee venom comprises about 40-50% of melittin or about 1.5 to 2.0% of hyaluronidase as taught by Bank *et al.* From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable of success in producing the claimed invention.

One having ordinary skill in the art at the time the invention was made would have been motivated to do this because Bank *et al* teaches Melittin has anti-inflammatory mechanism and this may be why therapeutic properties have long been attributed to bee venom, especially in arthritic conditions (Seep age 403, first paragraph, in particular). The term "comprising" is open-ended. It expands the claimed composition to include additional protein. Claims 43 and 44 are included in this rejection because the enzyme activity of Hayluronidase such as inhibiting gelatin induced aggregation of erythrocytes of about 3-5mm/H is the inherent properties of the enzyme itself and the dilution of enzyme such that it exhibits about 40 to 100HHU/ml is within the purview of one skill in the art as taught by Steigerwaldt *et al.*

Applicants' arguments filed 3/20/02 have been fully considered but are not found persuasive.

Applicants' position is that (1) Steigerwaldt does not explicitly teaches that its procaine hydrochoride is injected, (2) Steigerwaldt does not disclose the use of bee venom comprising about 40%-50% of melititin or about 1.5-2% of hyaluronidase in dry weight.

In response to Applicants argument that Steigerwaldt does not explicitly teaches that its procaine hydrochoride is injected, the base claim 31 recites administering to a patient "simultaneously" bee venom and at least one anesthetic. Steigerwaldt *et al* teach a method of administering bee venom to a patient suffering from a condition such as Rheumatoid arthritis comprising administering to a patient simultaneously between 0.06 mg and 1.62 mg per injection of bee venom intradermally which is about 0.01 mg and about 1.0 mg per injection and one local anesthetic such as procaine hydrochloride in an amount of 0.2%, (that is 0.2 g/100 ml or 2 mg/ml)

multiply by 0.1 cc or 0.1 ml per injection which is equivalent to 0.2 mg per injection which is about 0.3 mg per injection (See page 1047, column 1, Standardized Bee Venom, column 2 second paragraph, in particular). Since the reference composition has to be given simultaneously by injection, Steigerwaldt teaches that its procaine hydrochoride is injected. In response to Applicants argument that Steigerwaldt does not disclose the use of bee venom comprising about 40%-50% of melititin or about 1.5-2% of hyaluronidase in dry weight, Applicant is correct that Steigerwaldt does not disclose the use of bee venom comprising about 40%-50% of melititin or about 1.5-2% of hyaluronidase in dry weight. However, Bank *et al* teach commercially available bee venom is that of the common European honeybee Apis melifera and melittin is the major component of bee venom, which accounts for about 40%-50% in dry weight, and hyaluronidase accounts for about 1-2% in dry weight of the whole venom (See page 349, Melittin, page 344, Table II, page 337, in particular).

12. No claim is allowed.

13. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to "Neon" Phuong Huynh whose telephone number is (703) 308-4844. The examiner can normally be reached Monday through Friday from 9:00 am to 6:00 p.m. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any

inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

15. Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-7401.

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July 1, 2002

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